

In the Claims

Applicant has submitted a new complete claim set showing marked up claims with insertions indicated by underlining and deletions indicated by strikeouts and/or double bracketing.

Please cancel claims 55 without prejudice or disclaimer.

Please amend pending claims 1, 25, 27, 34, 46, 48-50 and 53 as noted below.

1. (Currently Amended) A device for generating an oscillating current, comprising:
 - an insulating layer positioned between at least two electrolyte reservoirs;
 - a negative bias electrode and a positive bias electrode, each electrode having one end in electrical communication with respective electrolyte reservoirs, the other ends of the electrodes being connected to a voltage source for applying a voltage and a current detector for measuring current;
 - at least one hole penetrating the insulating layer;
 - at least one pore positioned within each of the at least one hole, the at least one pore having a frequency of oscillation wherein the at least one pore oscillates between existing in one of an open and a closed state, wherein the closed state prevents ionic communication between the reservoirs and the open state allows ionic communication between the reservoirs to generate electrical current, the at least one pore being able to bind an analyte, wherein binding of the analyte to the at least one pore alters the frequency of oscillation from a first frequency to a second frequency.
2. (Original) A device as in claim 1, wherein the at least one hole has a diameter of less than about 1 μ m.
3. (Original) A device as in claim 1, wherein the at least one hole has a diameter of less than about 500 nm.
4. (Original) A device as in claim 1, wherein the at least one hole has a diameter of less than about 300 nm.

5. (Original) A device as in claim 1, wherein the at least one hole has a diameter of less than about 100 nm.
6. (Original) A device as in claim 1, wherein the at least one pore has a diameter of less than about 10 angstroms.
7. (Original) A device as in claim 1, wherein the at least one pore has a diameter of between about 3 angstroms and about 10 angstroms.
8. (Original) A device as in claim 1, further comprising the at least one pore being positioned in a lipid bilayer positioned within each of the at least one hole.
9. (Original) A device as in claim 8, wherein the at least one pore comprises the pore of an ion channel.
10. (Original) A device as in claim 8, wherein the ion channel comprises a closed ring arrangement of protein subunits.
11. (Original) A device as in claim 10, wherein the closed ring arrangement of protein subunits comprises at least 3 protein subunits.
12. (Original) A device as in claim 11, wherein the closed ring arrangement of protein subunits comprises between 3 and 15 protein subunits.
13. (Original) A device as in claim 12, wherein the closed ring arrangement of protein subunits comprises between 6 and 12 protein subunits.
14. (Original) A device as in claim 13, wherein each of the protein subunits is subunit c of ATP synthase.

15. (Original) A device as in claim 9, wherein the ion channel is selected from the group consisting of a sodium ion channel, a potassium ion channel, a calcium ion channel and combinations thereof.
16. (Original) A device as in claim 9, wherein the ion channel is a sodium/calcium ion channel.
17. (Original) A device as in claim 1, wherein the oscillation has a frequency of between about 0.1 Hz and about 700 Hz.
18. (Original) A device as in claim 1, wherein the current has a value of at least about 10 pA upon applying a voltage of between about 60 mV to about 100 mV.
19. (Original) A device as in claim 1, wherein the current has a value of at least about 50 pA upon applying a voltage of between about 60 mV to about 100 mV.
20. (Original) A device as in claim 1, wherein the current has a value of at least about 100 pA upon applying a voltage of between about 60 mV to about 100 mV.
21. (Original) A device as in claim 1, wherein the current has a value of at least about 200 pA upon applying a voltage of between about 60 mV to about 100 mV.
22. (Original) A device as in claim 1, further comprising an array of holes penetrating the insulating layer, and a separate electrolyte reservoir contacting each hole on at least one side of the insulating layer.
23. (Original) A device as in claim 22, wherein the array of holes is an n x m array and n and m can be the same or different and each of n and m is an integer of at least 2.

24. (Original) A device as in claim 1, further comprising an amplifier to amplify the generated electrical current.
25. (Currently Amended) A device for generating an oscillating current, comprising an oscillating ion channel having a frequency of oscillation, wherein the ion channel is positioned within a membrane spanning a hole having a diameter less than 1 μm , the oscillating ion channel being able to bind an analyte, wherein binding of the analyte to the oscillating ion channel alters the frequency of oscillation from a first frequency to a second frequency.
26. (Original) A device as in claim 1, wherein the at least one hole has one common electrolyte reservoir.
27. (Currently Amended) A method, comprising:
providing at least one membrane positioned between two electrolyte reservoirs, the membrane having at least one oscillating ion channel; and
measuring an first electrical output from the oscillating ion channel in the membrane;
allowing the at least one oscillating ion channel to bind to an analyte; and
measuring a second electrical output from the oscillating ion channel in the membrane different from the first electrical output.
28. (Original) A method as in claim 27, wherein the ion channel oscillates steadily for at least 1 day.
29. (Original) A method as in claim 27, wherein the ion channel is selected from the group consisting of a sodium ion channel, a potassium ion channel, a calcium ion channel and combinations thereof.

30. (Original) A method as in claim 29, wherein the ion channel is a sodium/calcium ion channel.
31. (Original) A method as in claim 30, wherein the sodium/calcium ion channel is formed from a closed ring arrangement of protein subunits.
32. (Original) A method as in claim 31, wherein each of the protein subunits is subunit c of ATP synthase.
33. (Original) A method as in claim 30, wherein each of the protein subunits is stable for a period of at least one day upon being stored in an organic solvent under an ambient atmosphere.
34. (Currently Amended) A sensor, comprising:
 - an insulating layer positioned between two electrolyte reservoirs;
 - a negative bias electrode and a positive bias electrode, each electrode having one end in electrical communication with respective electrolyte reservoirs, the other ends of the electrodes being connected to a voltage source for applying a voltage and a current detector for measuring current;
 - at least one hole penetrating the insulating layer; and
 - an oscillating ion channel having a frequency of oscillation positioned within the hole, the oscillating ion channel being able to bind an analyte, wherein binding of the analyte to the oscillating ion channel alters the frequency of oscillation from a first frequency to a second frequency.
35. (Original) A sensor as in claim 34, further comprising one of the two electrolyte reservoirs being exposed to an atmosphere suspected of containing the analyte.
36. (Original) A method for detecting a sample of analyte, comprising:
 - providing at least one ion channel oscillating at a first frequency;

allowing the sample to bind to the at least one ion channel to cause the ion channel to oscillate at a second frequency; and
measuring the second frequency.

37. (Original) A method as in claim 36, wherein the providing step further comprises:
 - positioning the at least one ion channel into each of the at least one hole penetrating an insulating layer, the insulating layer being positioned between two electrolyte reservoirs; and
 - immersing one end of each of a negative bias electrode and a positive bias electrode into respective electrolyte reservoirs, the other ends of the electrodes being connected to a voltage source for applying a voltage and a detector for measuring current.
38. (Original) A method as in claim 36, wherein a time between the binding and measuring the second frequency is less than about 1 s.
39. (Original) A method as in claim 36, wherein a time between the binding and measuring the second frequency is less than about 500 ms.
40. (Original) A method as in claim 36, wherein a time between the binding and measuring the second frequency is less than about 100 ms.
41. (Original) A method as in claim 36, wherein the amount of analyte in the sample is less than about 1 nM.
42. (Original) A method as in claim 36, wherein the amount of analyte in the sample is less than about 500 pM.
43. (Original) A method as in claim 36, wherein the amount of analyte in the sample is less than about 100 pM.

44. (Original) A method as in claim 36, further comprising derivatizing the ion channel with functional groups to detect a predetermined analyte.

45. (Original) A method as in claim 36, wherein the first frequency is at least 0.1 Hz.

46. (Currently Amended) A device comprising:
an ion channel capable of oscillation at an oscillation frequency, wherein binding of the ion channel to an analyte alter the oscillation frequency from a first frequency to a second frequency; and
an electrical amplifier in electrical communication with the ion channel.

47. (Original) A device as in claim 46, further comprising an electrical insulator, wherein the ion channel is located in a hole in the barrier passing from a first side of the insulator to a second side of the insulator, the device further comprising first and second electrolyte reservoirs positioned on respective sides of the barrier and contacting first and seconds ends of the hole, and electrical circuitry constructed and arranged to apply potential across the hole and to measure a change in electrical characteristic resulting in a change in oscillation frequency of the ion channel, amplified by the amplifier.

48. (Currently Amended) A device comprising:
a barrier having a first side and a second side;
a pore in the barrier, existing in one of having a frequency of oscillation wherein the pore oscillates between an open and a closed state, the closed state preventing ionic communication across the pore and the open state allowing ionic communication across the pore from the first side of the barrier to the second side of the barrier, the pore being able to bind an analyte, wherein binding of the analyte to the pore alters the frequency of oscillation from a first frequency to a second frequency;
a first electrolyte container, constructed and arranged to contain an electrolyte and to position the electrolyte in contact with the a first side of the pore, including container interior walls integral with the barrier; and

a second electrolyte container, constructed and arranged to contain an electrolyte and to position the electrolyte in contact with a second side of the pore, including container interior walls integral with the barrier.

49. (Currently Amended) A device comprising:

a barrier having a first side and a second side;
a pore in the barrier, existing in one of having a frequency of oscillation wherein the pore oscillates between an open and a closed state, the closed state preventing ionic communication across the pore and the open state allowing ionic communication across the pore from the first side of the barrier to the second side of the barrier, the pore being able to bind an analyte, wherein binding of the analyte to the pore alters the frequency of oscillation from a first frequency to a second frequency;

a first electrolyte container, constructed and arranged to contain an electrolyte and to position the electrolyte in contact with the a first side of the pore; and

a second electrolyte container, constructed and arranged to contain an electrolyte and to position the electrolyte in contact with a second side of the pore, and fastenable to the first electrolyte container.

50. (Currently Amended) A device comprising:

a barrier having a first side and a second side;
a pore in the barrier, existing in one of having a frequency of oscillation wherein the pore oscillates between an open and a closed state, the closed state preventing ionic communication across the pore and the open state allowing ionic communication across the pore from the first side of the barrier to the second side of the barrier, the pore being able to bind an analyte, wherein binding of the analyte to the pore alters the frequency of oscillation from a first frequency to a second frequency;

a first electrolyte container, fastenable to the barrier, constructed and arranged to contain an electrolyte and to position the electrolyte in contact with a first side of the pore; and

a second electrolyte container, fastenable to the barrier, constructed and arranged

to contain an electrolyte and to position the electrolyte in contact with a second side of the pore.

51. (Previously Presented) A device as in claim 50, wherein the barrier includes an electrical insulator.
52. (Original) A method for generating at least one oscillating current, comprising providing at least two separate membranes positioned adjacent at least one electrolyte reservoir, each membrane having at least one oscillating ion channel, and simultaneously measuring an electrical output from the at least one oscillating ion channel in each membrane.
53. (Currently Amended) A device comprising:
 - a first electrolyte reservoir;
 - a second electrolyte reservoir;
 - electrical circuitry connecting the first and second electrolyte reservoirs; and
 - subunit c of ATP synthase or a derivative thereof, the subunit or derivative thereof able to bind to an analyte and separating first and second electrolyte reservoirs.
54. (Previously Presented) A device as in claim 53, including a hole spanned by an insulating membrane containing a pore.
55. (Cancelled)